Highlights from ACC/I2 2009
Structural Heart Disease

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Disclosures

Equity

- None

Grant Support/Drugs

- Eli Lilly - Schering-Plough
- Baxter

Grant Support/Devices

- Boston Scientific - Edwards Lifesciences
- MedRAD

Consulting/Advisory Boards

- Cordis - Medtronic

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PROTECT AF Trial: Randomized Prospective Trial of Percutaneous LAA Closure vs Warfarin for Stroke Prevention in AF ACC & i2 Summit 2009

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Relevant Financial Relationship(s)
Mayo receives research support from Atritech and may receive royalties

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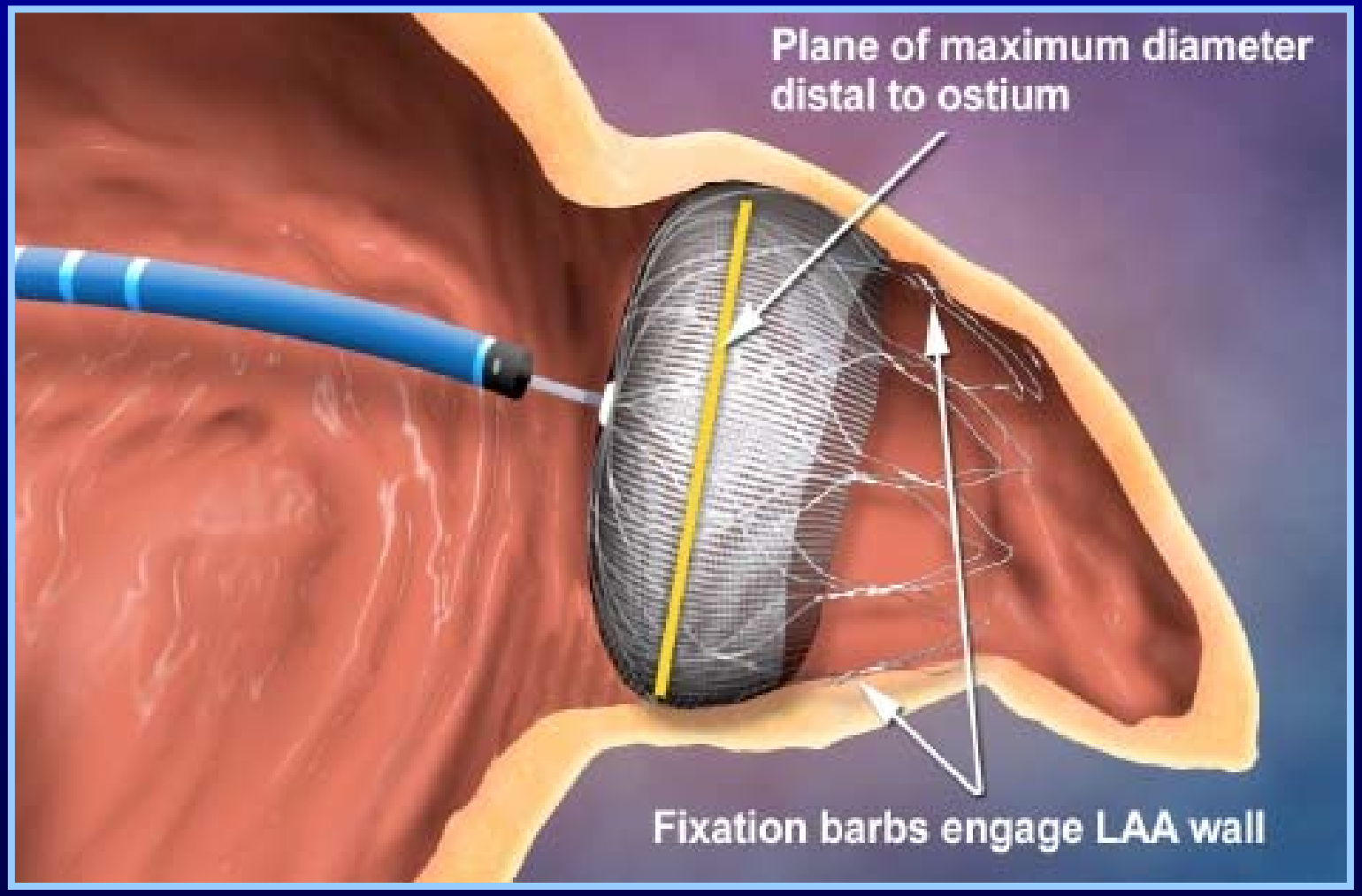
Challenges in Treating AF

- Warfarin is the cornerstone of therapy for stroke prevention
  - 60-70% risk reduction vs. no therapy
  - 30-40% risk reduction vs. ASA
- However warfarin is not always well-tolerated
  - Narrow therapeutic range (INR between 2.0 – 3.0)
  - Effectiveness is impacted by interactions with some foods and medications
  - Requires frequent monitoring and dose adjustments
- Less than 50% of eligible patients are treated with warfarin due to tolerance or non-compliance issues

WATCHMAN LAA Closure Device



PROTECT AF Clinical Trial Design

- Prospective, randomized study of WATCHMAN LAA Device vs. Long-term Warfarin Therapy
- 2:1 allocation ratio device to control
- 800 Patients enrolled from Feb 2005 to Jun 2008
  - Device Group (463)
  - Control Group (244)
  - Roll-in Group (93)
- 59 Enrolling Centers (U.S. & Europe)

PROTECT AF Trial Endpoints

Primary Efficacy Endpoint

- Composite of CV death, stroke (ischemic or hemorrhagic), or systemic embolism

Primary Safety Endpoint

- Device embolization requiring retrieval
- Pericardial effusion requiring intervention
- Cranial bleeds and gastrointestinal bleeds
- Any bleed that requires ≥ 2uPRBC

Warfarin Discontinuation

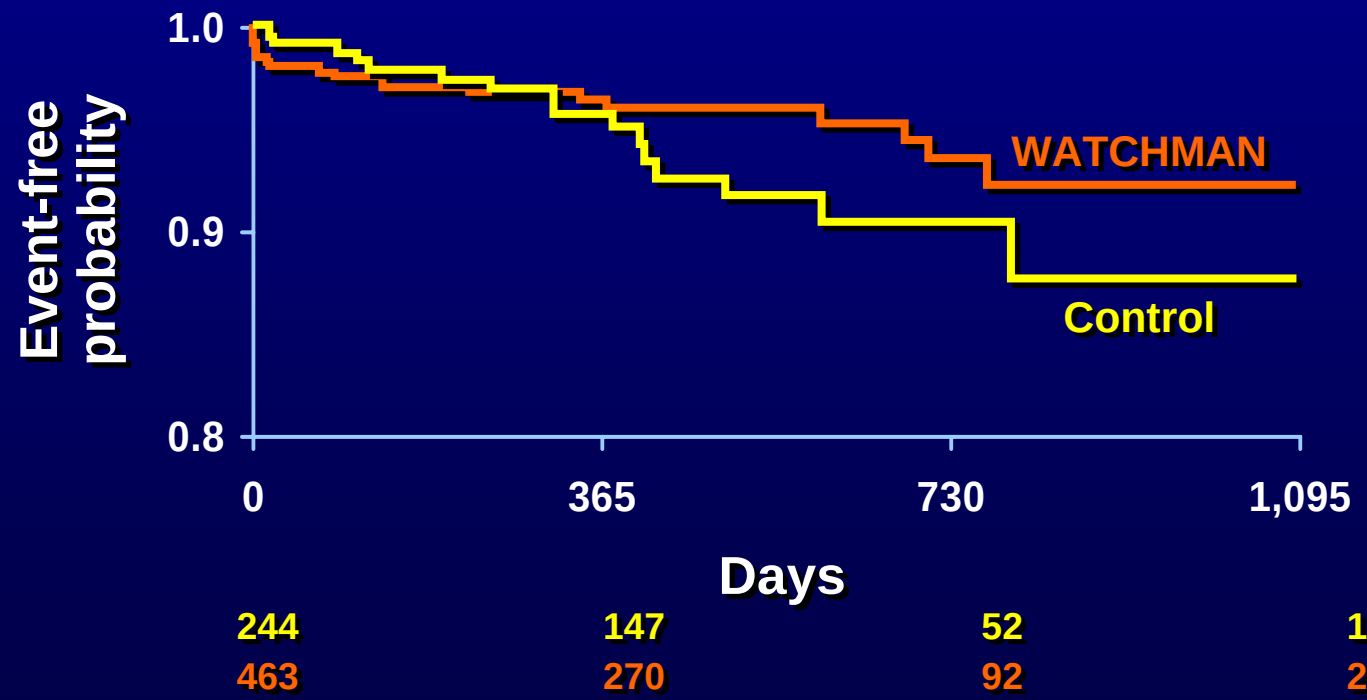
87% of implanted subjects were able to cease warfarin at 45 days and the rate further increased at later time points

Visit	Watchman N/Total (%)
45 day	349/401 (87.0)
6 month	347/375 (92.5)
12 month	261/280 (93.2)
24 month	95/101 (94.1)

- **Reasons for remaining on warfarin therapy after 45-days:**
  - **Observation of flow in the LAA (n = 30)**
  - **Physician Order (n = 13)**
  - **Other (n = 9)**

Primary Efficacy Results:
Freedom from CV Death/Stroke/Systemic Embolism

	Device			Control		
	Events (no.)	Total pt-yr	Rate	Events (no.)	Total pt-yr	Rate
	20	582	3.4%/yr	16	318	5.0%/yr



ITT Cohort:
Non-inferiority criteria met

Posterior Probability:
Non-Inferiority = 99.8%
Superiority = 83.0%

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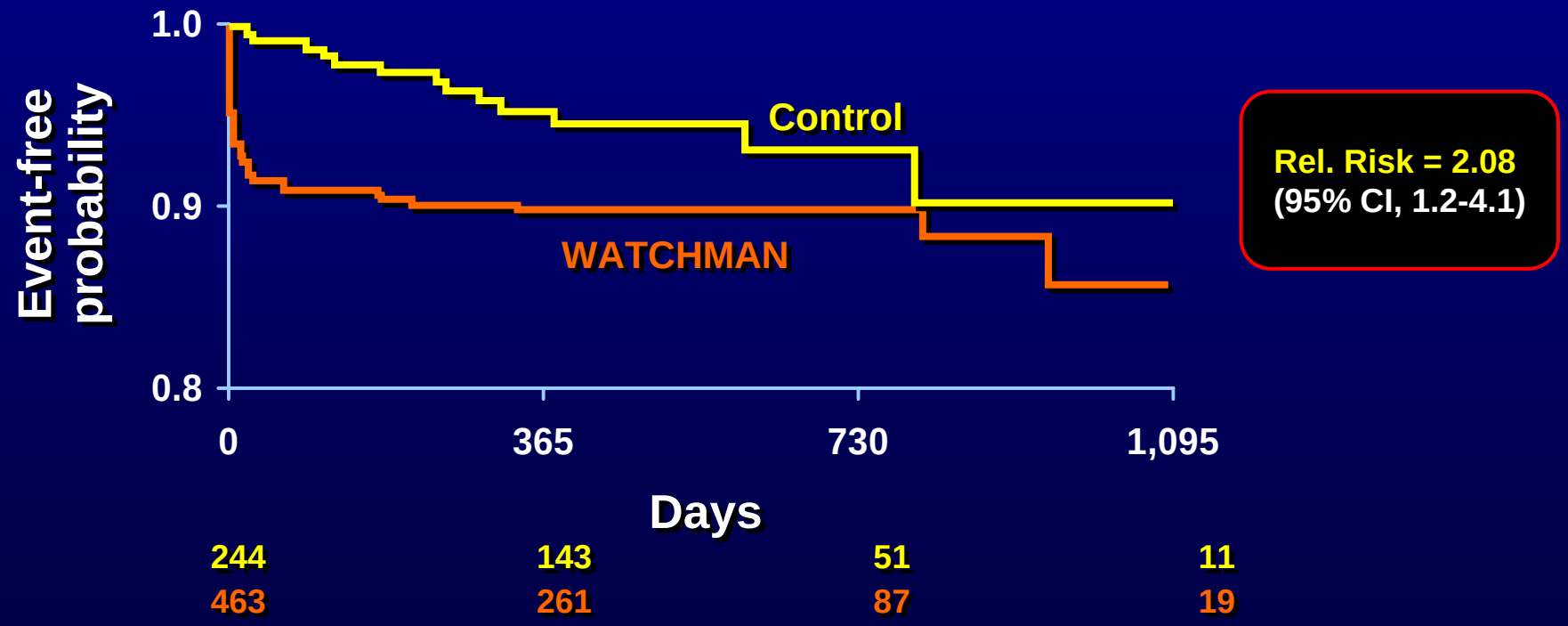
3001664-2

Primary Safety Results

Device Embolization, Pericardial Effusion, Major Bleed

Device			Control		
Events (no.)	Total pt-yr	Rate (95% CI)	Events (no.)	Total pt-yr	Rate (95% CI)
48	554.2	8.7	13	312.0	4.2



Rel. Risk = 2.08
(95% CI, 1.2-4.1)

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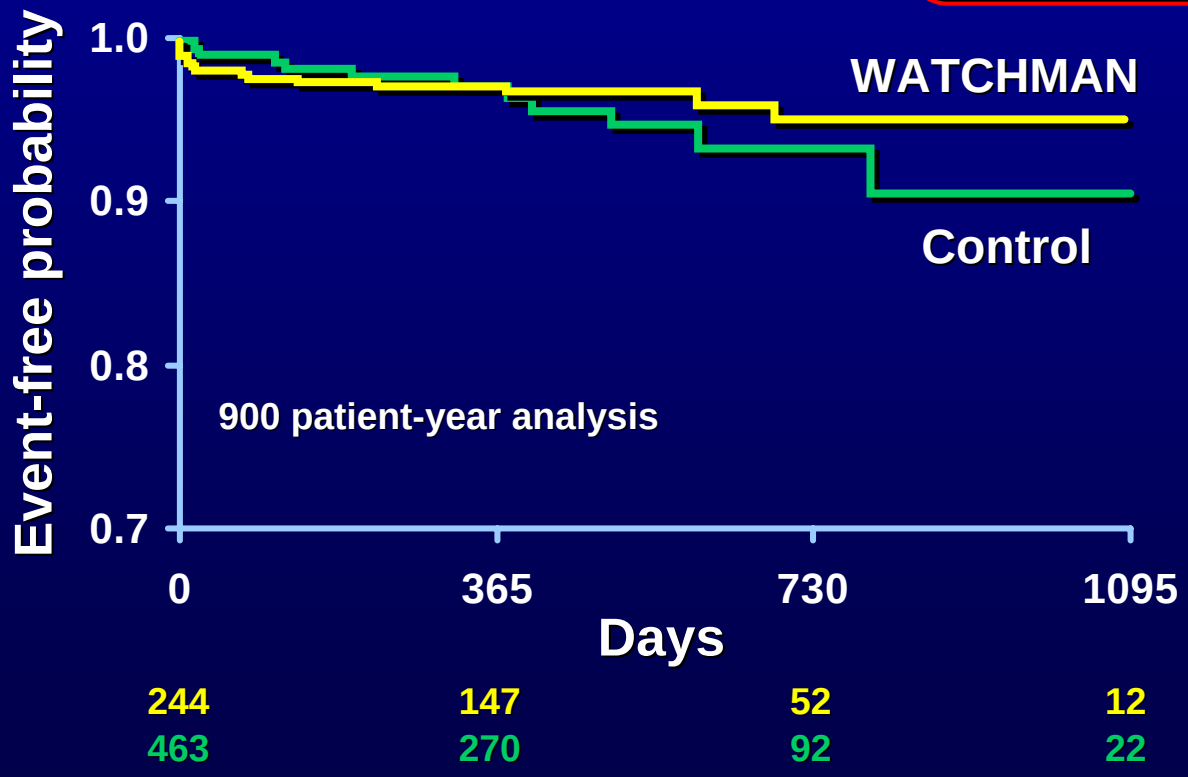
Freedom from Any Stroke

Device			Control		
Events (no.)	Total pt-yr	Rate (95% CI)	Events (no.)	Total pt-yr	Rate (95% CI)
15	583	2.6%/yr	11	318	3.5%/yr



Rel. Risk = 0.7
(95% CI, 0.4-1.8)

Posterior Probability:

Non-Inferiority = 99.8%
Superiority = 73.1%

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Procedural Learning Curve
Impact on Pericardial Effusions

- Throughout PROTECT AF Trial, procedural modifications and training enhancements were implemented

Site implant group	Any		Serious	
	No.	%	No.	%
Early patients (1-3)	13/154	8.4	10/154	6.5
Late patients (≥4)	27/388	7.0	17/388	4.4
Total	40/542	7.2	27/542	5.0

- Continued ACCESS Registry

Any		Serious	
No.	%	No.	%
1/88	1.1	1/88	1.1

Implications

- LAA occlusion with the Watchman device may be a reasonable alternative to warfarin for many patients who are candidates for systemic anticoagulation
- ? Role of LAA occlusion in patients at high risk of stroke who cannot tolerate warfarin

Health Related Quality of Life and U.S. Economic Outcomes of PCI with Drug-Eluting Stents vs. Bypass Surgery: *1-Year Results from the SYNTAX Trial*

David J. Cohen, Tara A. Lavelle, Patrick W. Serruys, Friedrich W. Mohr, Haiyan Li, Yang Lei, Kaijun Wang, Kate Robertus, Elizabeth M. Mahoney, Yueping Zhu, Keith D. Dawkins, A. Pieter Kappetein
on behalf of the SYNTAX Investigators

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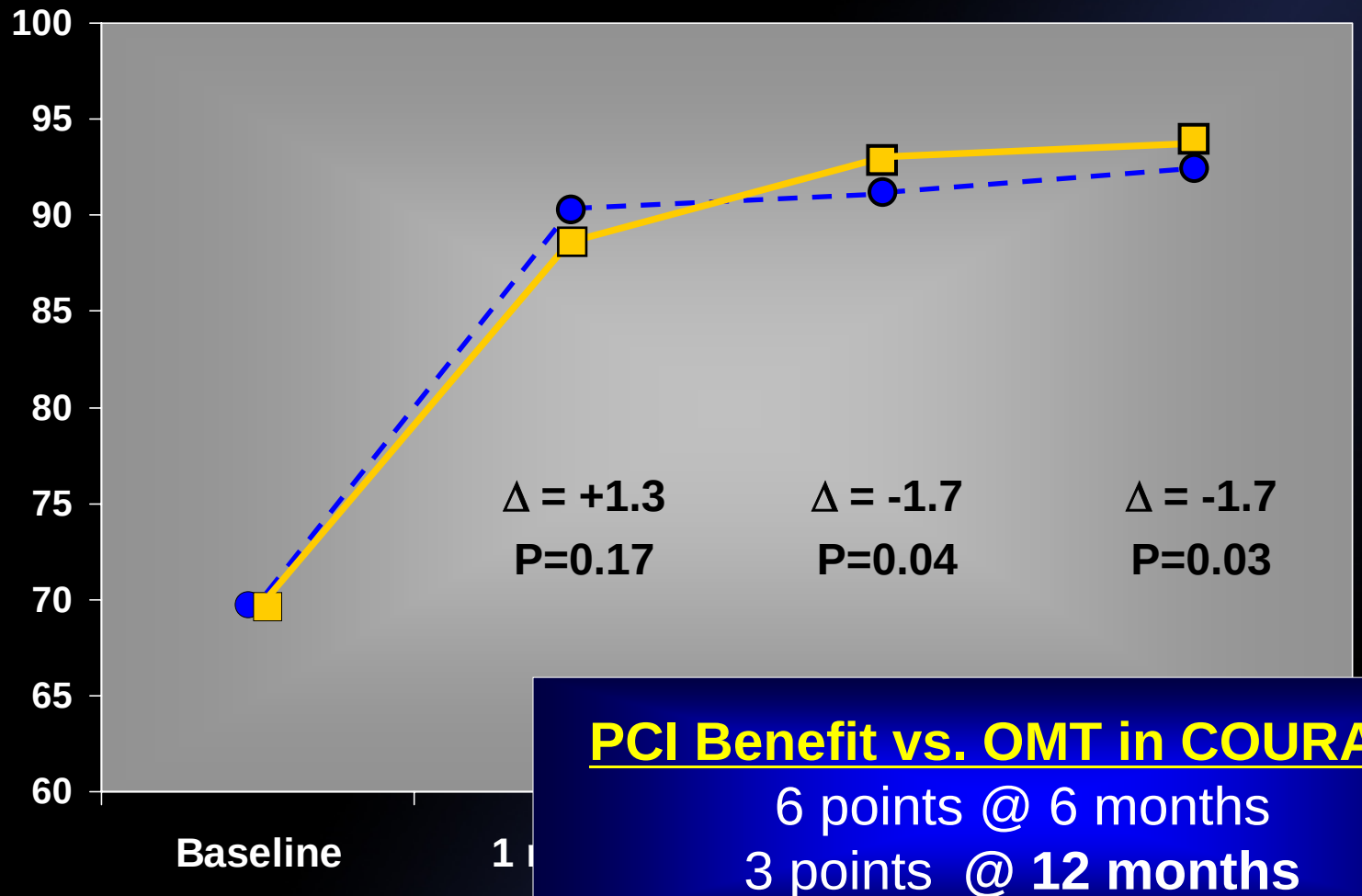
Background

- Recently 1-year results from the SYNTAX trial have demonstrated that for patients with left main or 3-vessel disease, CABG results in lower rates of MACCE than PCI with DES-- driven by a significant reduction in the need for repeat revascularization
- Since there were no overall differences in irreversible endpoints, however, quality of life and economic factors should be important considerations in determining the optimal treatment for these highly prevalent conditions
- To address these issues, both quality of life and health economic analyses were included in the design of the SYNTAX trial

Primary QOL Endpoint:
SAQ-Angina Frequency

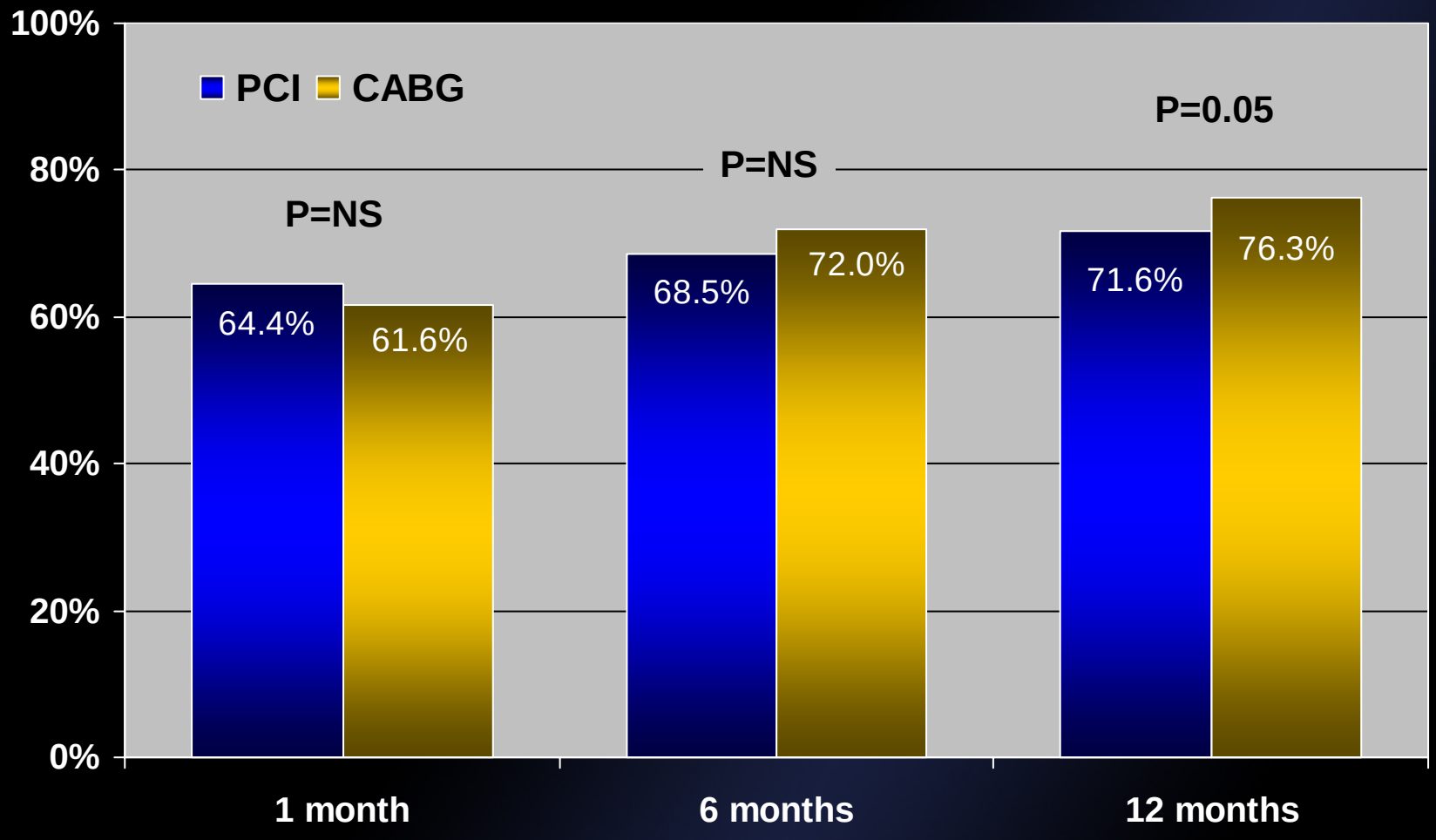


PCI Benefit vs. OMT in COURAGE

6 points @ 6 months

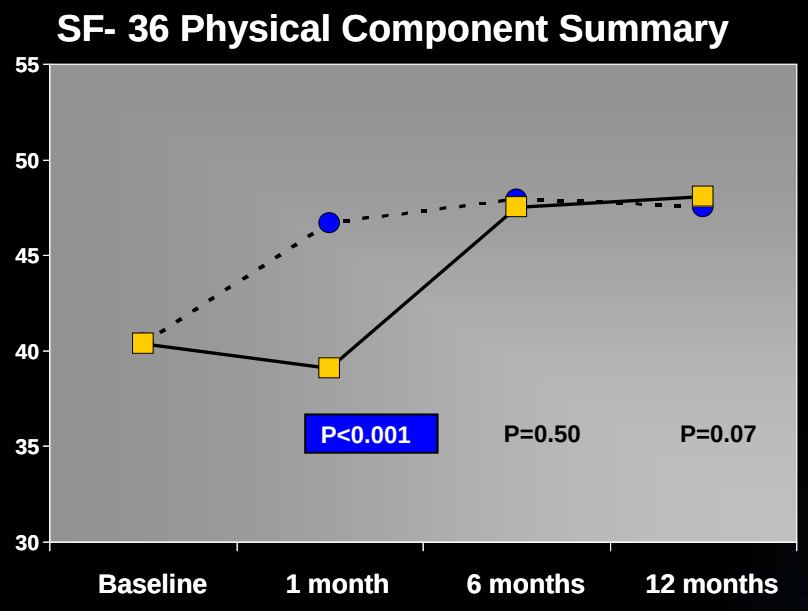
3 points @ **12 months**

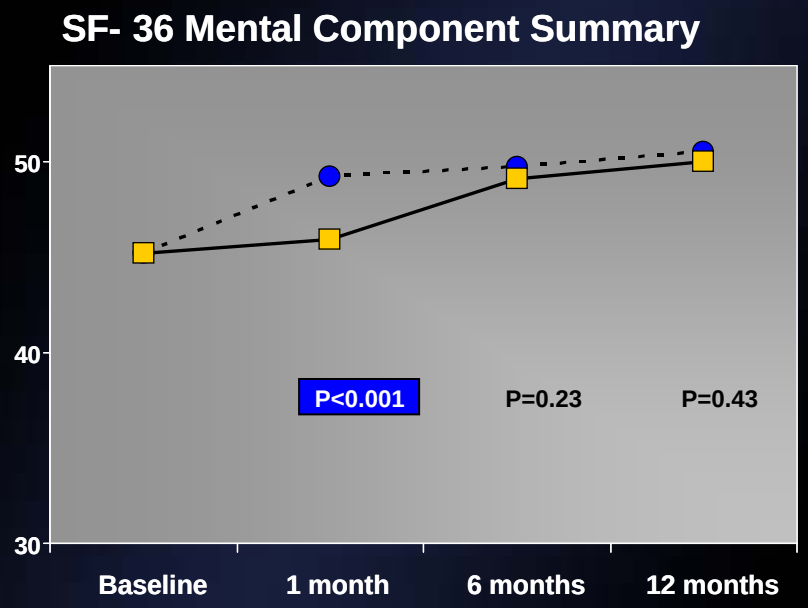
SAQ-AF: Angina-Free*

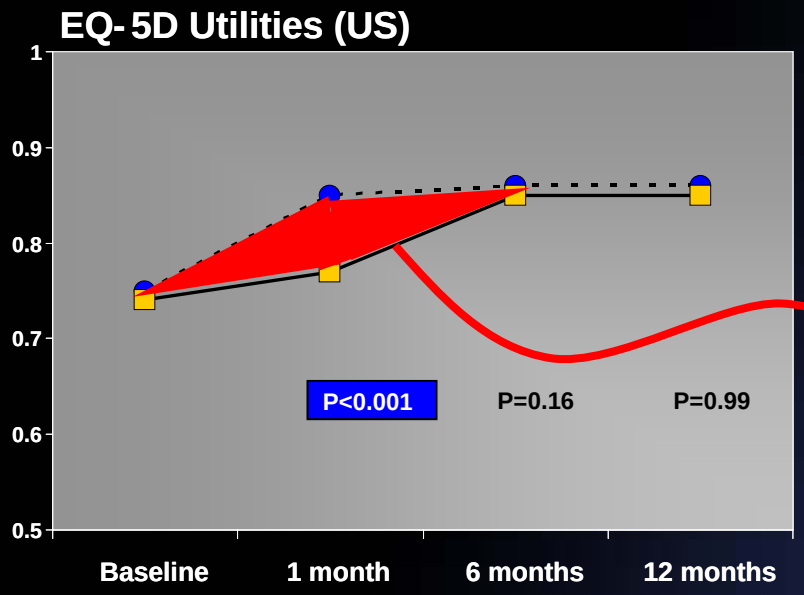


* Defined as SAQ-AF score = 100

Generic QOL and Utilities







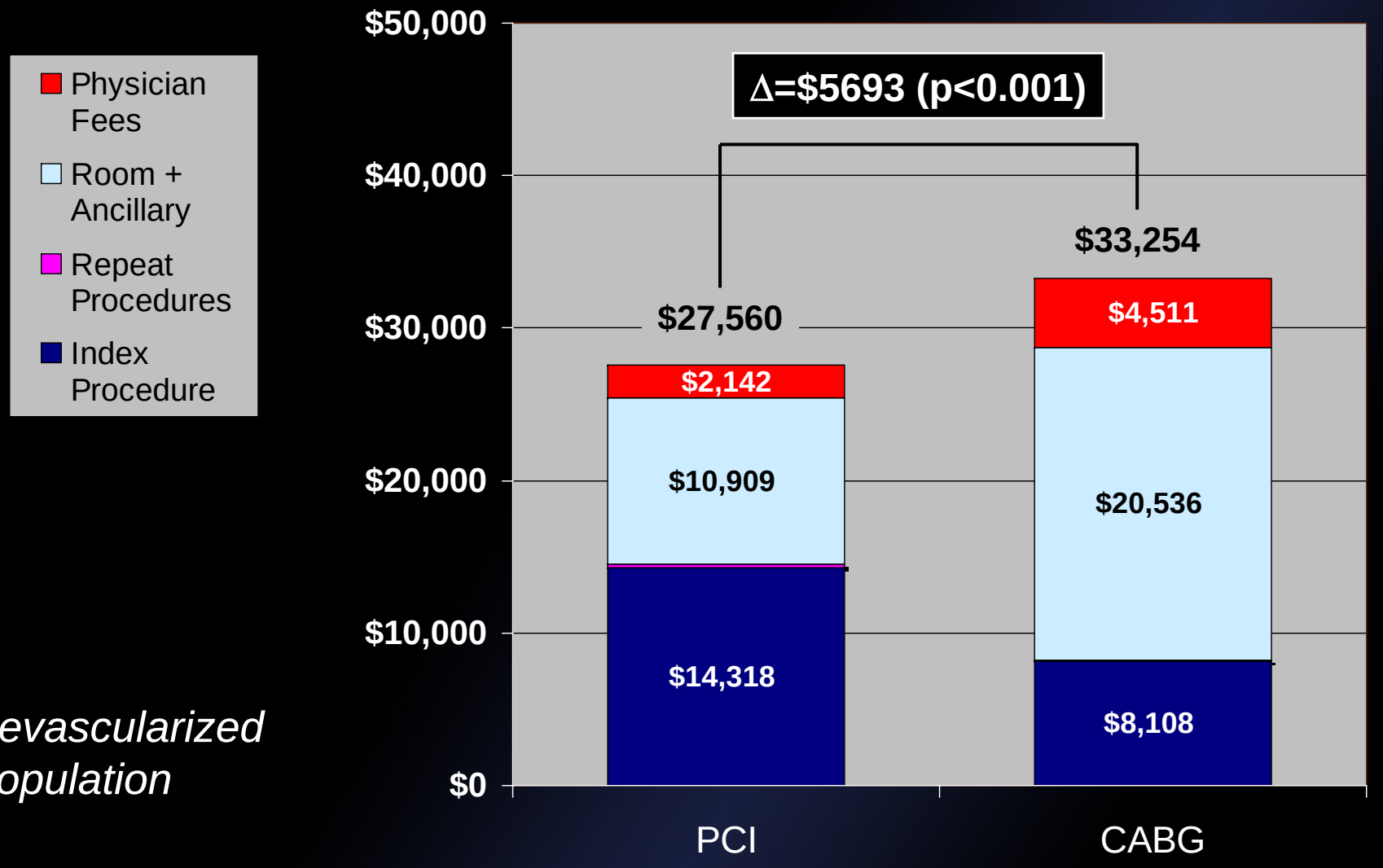
PCI

CABG

Quality Adjusted Life Years

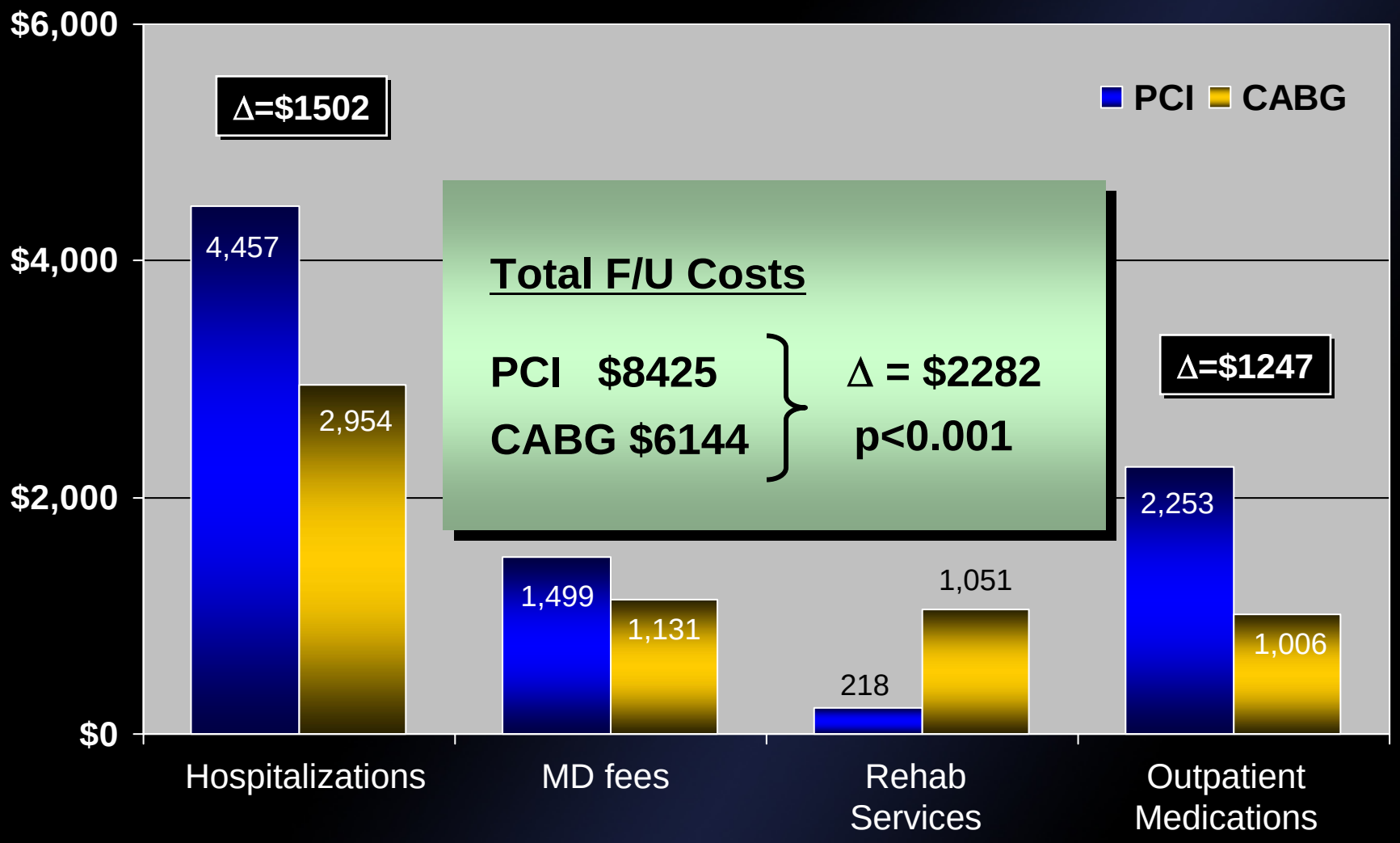
Δ = 0.02 (P<0.01)

Initial Hospitalization Costs

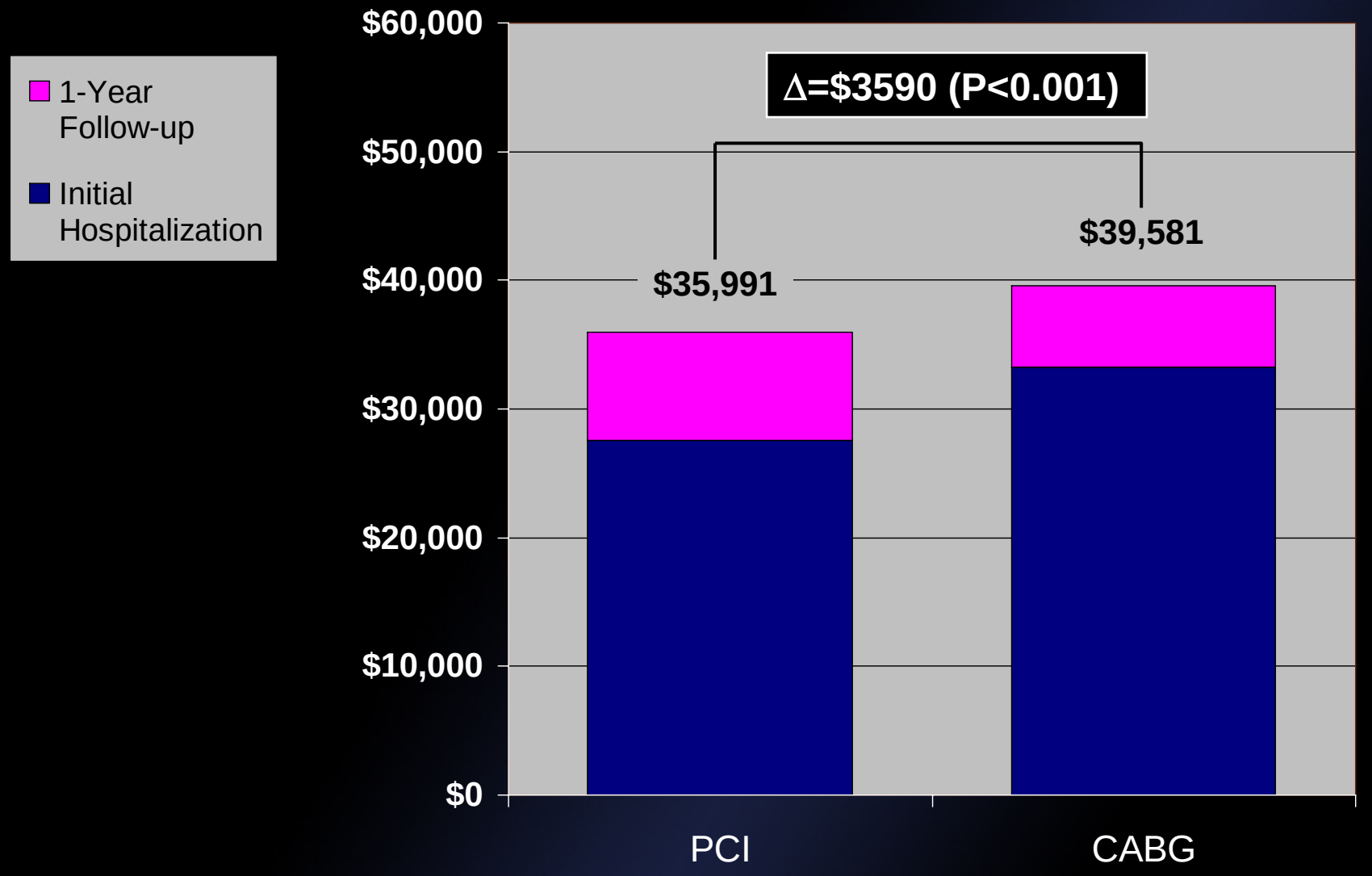


Revascularized Population

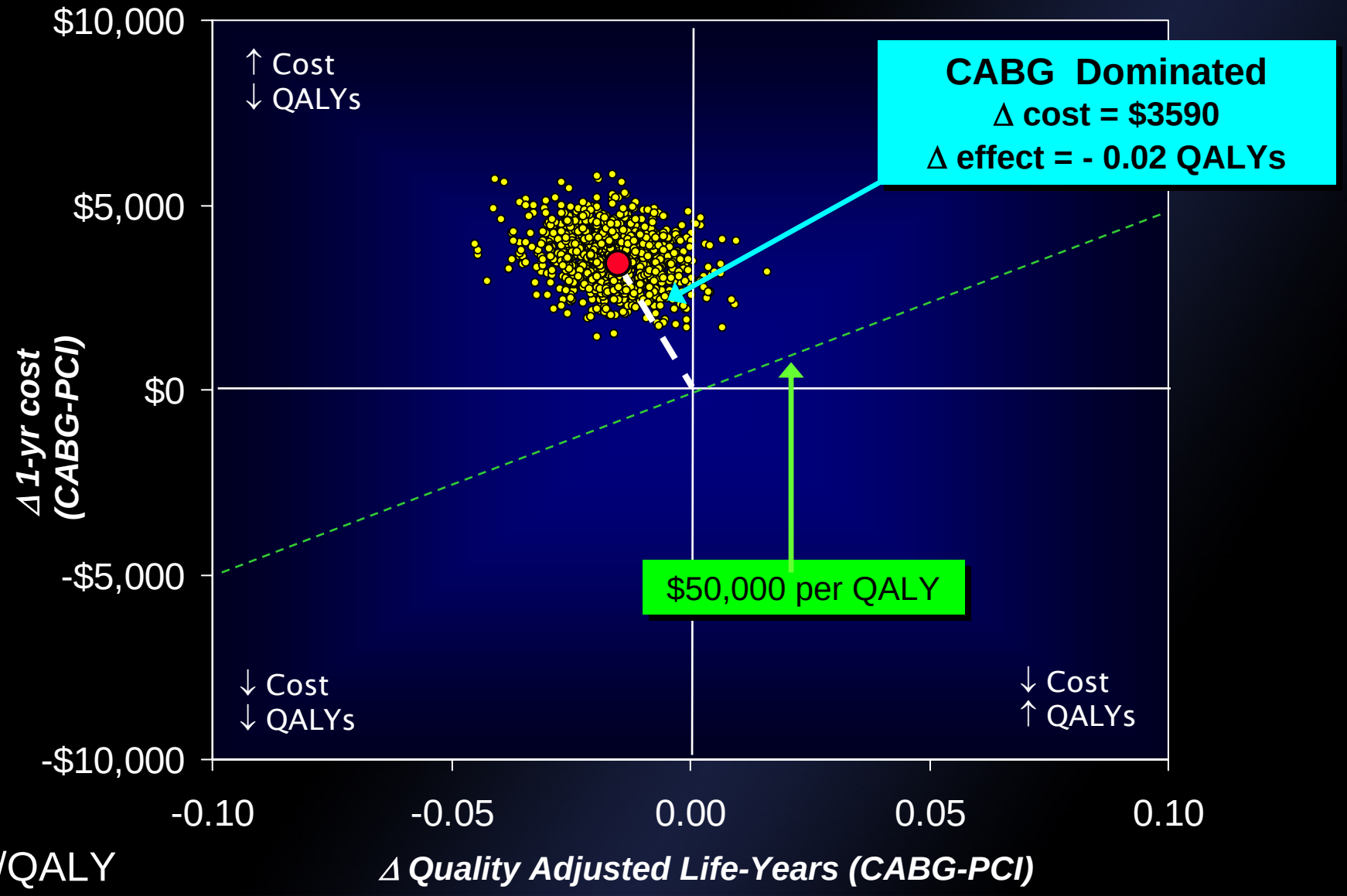
Follow-up Costs



Total 1-Year Costs

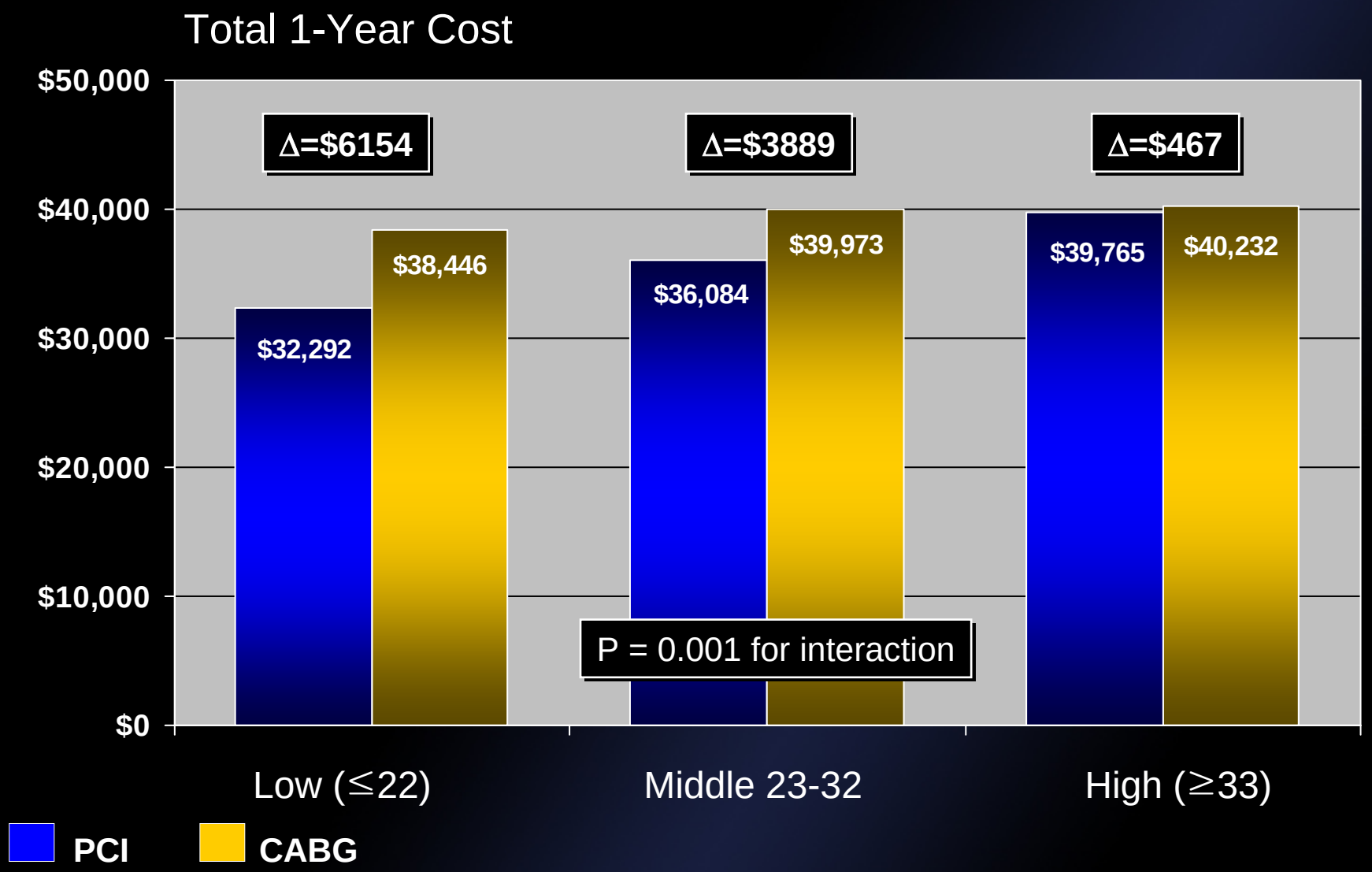


Cost-Effectiveness of CABG vs. PCI*
Overall Population



*$/QALY

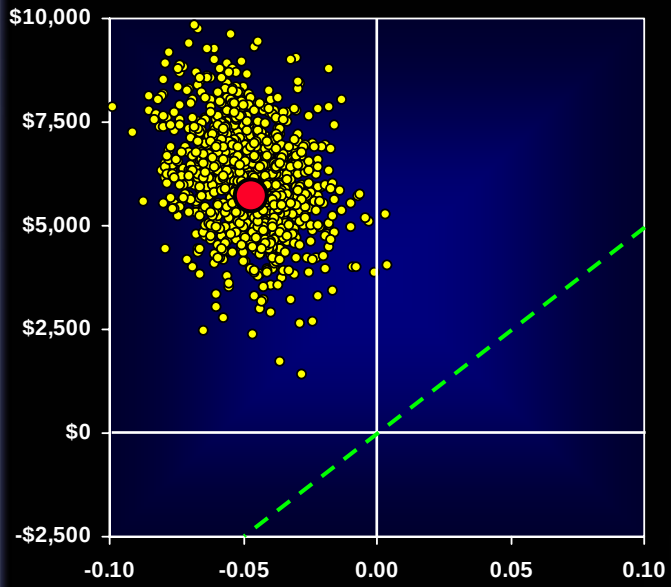
Subgroup Analysis:
SYNTAX Score Tertiles



Cost-Effectiveness of CABG vs. PCI ($/QALY)

SYNTAX Score Tertiles

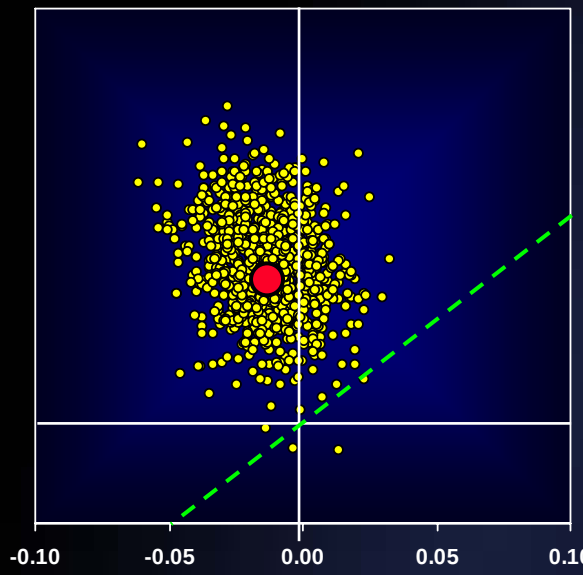
Low (≤22)



Δ Cost	$6154
Δ QALY	-0.047
ICER	Dominated

Pr <$50K/QALY = 0.0%

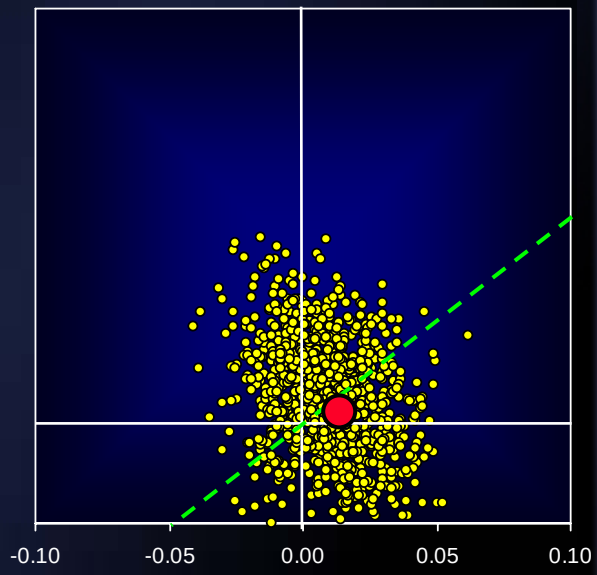
Mid (23-32)



Δ Cost	$3889
Δ QALY	-0.013
ICER	Dominated

Pr <$50K/QALY = 0.3%

High (≥33)



Δ Cost	$467
Δ QALY	+0.010
ICER	$43,000/QALY

Pr <$50K/QALY = 49%

Summary

- Angina relief was slightly better with CABG at 1-year, but the extent of benefit was small and below the threshold generally considered clinically important
- All other QOL endpoints favored PCI at 1 month- but were comparable at 6 and 12 months
- Consistent with the overall clinical results, the cost-effectiveness of PCI vs. CABG at 1-year differed substantially according to pt characteristics--particularly angiographic complexity
- Longer-term follow-up is essential to fully assess both QOL and cost-effectiveness for these challenging populations